

AMENDMENTS TO THE CLAIMS:

Claim 1 (Currently Amended): A process for the purification of olanzapine characterized in that said process comprises the following steps:

- a) mixing olanzapine with an organic acid in an organic solvent or a mixture of organic solvents to form an olanzapine acid addition salt,
 - b) precipitating and isolating the olanzapine acid addition salt and,
 - c) ~~transformation~~ transforming ~~of~~ the olanzapine acid addition salt to olanzapine, wherein the transformation step comprises the following substeps:
 - i) dissolving ~~an~~ the acid addition salt of olanzapine in water to make a solution thereof ~~to form an aqueous solution thereof~~,
 - ii) adjusting the pH of the obtained ~~aqueous~~ solution to about 8-10,
 - iii) contacting the adjusted pH aqueous solution with an organic solvent to form a separate water phase and organic solvent phase;
 - ~~iiiiv)~~ iv) extracting olanzapine from the ~~aqueous~~ water phase to ~~an~~ the organic solvent phase; and
 - ~~ivv)~~ v) isolating ~~the acid addition salt of~~ olanzapine from the organic solvent phase by concentrating the ~~solution to form olanzapine salt crystals therein~~ organic solvent phase to cause olanzapine crystals to form therein and separating and separation of the crystals of the aforementioned salt of olanzapine therefrom from the organic solvent phase;
- wherein the olanzapine crystals include less than 0.05 % of piperazine 1,4-bis-4-yl-(2-methyl)-10H-thieno-[2,3-b][1,5]benzodiazepine.

Claim 2 (Currently Amended): The process according to claim 1 wherein the organic acid in step (a) is selected from the group consisting of ~~one or more~~ sulfonic acids ~~or one or more~~ and carboxylic acids.

Claim 3 (Currently Amended): The process according to claim 2 wherein the ~~one or more~~ carboxylic acid[[s]] ~~are~~ is selected from the group consisting of ~~one or more of~~ fumaric acid and benzoic acid.

Claim 4 (Currently Amended): The process according to claim 1 wherein the organic solvent in step (a) is selected from the group consisting of ~~one or more of~~ tetrahydrofuran, acetone, dimethylformamide and acetonitrile.

Claim 5 (Previously Presented): The process according to claim 1 wherein the mixture of organic solvents in step (a) is a mixture of tetrahydrofuran with at least one polar solvent.

Claim 6 (Currently Amended): The process according to claim 5 wherein said polar solvent is selected from the group consisting of ~~one or more of~~ dimethylformamide, dimethylacetamide, N-methylpyrrolidone, 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone, 1,3-dimethyl-2-imidazolidinone, tetramethylurea, dimethyl sulfoxide, sulfolane, acetone and acetonitrile.

Claims 7-21 (Cancelled)

Claim 22 (Currently Amended): A process for the preparation of olanzapine ~~in the form of an acid addition salt~~ characterized in that said process comprises the following steps:

- a) reacting 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride with N-methylpiperazine to yield olanzapine and
- b) ~~transforming~~ converting the obtained olanzapine to an acid addition salt thereof, ~~wherein the transformation step comprises the following substeps:~~
 - i) ~~diluting the obtained reaction mixture with water,~~
 - ii) ~~extracting the diluted reaction mixture with an organic solvent, wherein the organic solvent is selected from the group consisting of ketones, chlorinated hydrocarbons, and mixtures thereof,~~
 - iii) ~~evaporating the organic phase and diluting the residue with a second solvent to obtain a solution containing the residue,~~
 - iv) ~~adding an organic acid to the solution containing the residue to precipitate olanzapine acid addition salt therefrom and~~
 - v) ~~isolating precipitated olanzapine acid addition salt by formation and separation of crystals from the solution; and~~
- c) transforming the olanzapine acid addition salt to olanzapine, wherein the transformation comprises the following substeps:

i) dissolving the acid addition salt of olanzapine in water to form an aqueous solution thereof;

ii) adjusting the pH of the aqueous solution to about 8-10,

iii) contacting the adjusted pH aqueous solution with an organic solvent to form a water phase and an organic phase;

iv) extracting olanzapine from the water phase to the organic solvent phase;

v) isolating olanzapine from the organic solvent phase by concentrating the solution to cause formation of crystals of olanzapine therein followed by separation of the crystals therefrom; and

wherein the olanzapine crystals include less than 0.05 % of piperazine 1,4-bis-4-yl-(2-methyl)-10H-thieno-[2,3-b][1,5]benzodiazepine.

Claim 23 (Cancelled).

Claim 24 (Currently Amended): A process for the preparation of olanzapine ~~in the form of an acid addition salt~~ characterized in that said process comprises the following steps:

a) reacting N-desmethyloanzapine is reacted with a methylating agent to yield a reaction mixture containing olanzapine,

b) diluting the obtained reaction mixture is diluted with water and ~~acidified~~ acidifying the mixture, as necessary, with an acid,

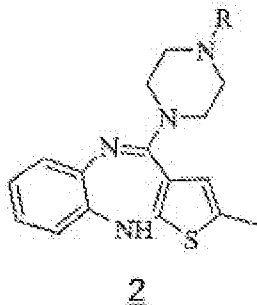
c) adding to the reaction mixture, a chlorinated organic solvent is added to provide separable aqueous to the diluted reaction mixture to induce formation of separate acidic water and organic solvent phases ~~which wherein olanzapine is contained in the water phase are then separated,~~

d) separating the water and organic solvent phases;

e) neutralizing the obtained aqueous water phase is neutralized and extracting olanzapine is extracted therefrom with a chlorinated organic solvent to obtain the organic solvent phase containing olanzapine and

ef) adding an organic acid or substituted organic acid or an organic acid derivative of formula RX; wherein R represents an organic radical and X is selected from a group of Cl, Br or

I; or an organic acid anhydride; ~~is added~~ to the organic phase to form a N substituted N-desmethylolanzapine derivative of formula 2



~~fg) optionally evaporating the obtained organic solvent phase is optionally evaporated and~~
diluting the residue is diluted with a second organic solvent,

~~gh) adding an organic acid is added~~ either to the ~~obtained~~ diluted residue solution containing the second organic solvent ~~and residue therein~~ or directly to the olanzapine extract from ~~the said extraction in~~ step (d), and

~~hi) precipitated precipitating an~~ olanzapine acid addition salt ~~is isolated by separation of the~~ in the form of crystals from the material to which an organic acid was added in step h; and

~~ij) transformation of transforming the olanzapine acid addition salt to olanzapine, wherein~~
the transformation step comprises the following substeps:

- 1) dissolving an acid addition salt of olanzapine in water,
- 2) adjusting pH of the obtained solution to about 8-10,
- 3) extracting olanzapine from the water phase to the organic solvent phase and
- 4) isolating the acid addition salt of olanzapine from the organic solvent phase by concentrating the solution and separation of the crystals

wherein the obtained olanzapine includes less than 0.05 % of piperazine 1,4-bis-4-yl-(2-methyl)-10H-thieno-[2,3-b][1,5]benzodiazepine.

Claim 25 (Cancelled)

Claim 26 (Previously Presented): The process according to claim 24 wherein said chlorinated organic solvent is methylene chloride.

Claim 27 (Original): The process according to claim 24 wherein the organic solvent in steps (c) and (d) is methylene chloride and said second solvent in step (f) is methanol.

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Claims 28-34 (Cancelled)

Claim 35 (Currently Amended): Olanzapine prepared according to the processes disclosed in claim 1 characterized in that the ~~detectible~~ N-desmethyloanzapine content, if any, in the final product of olanzapine is less than 0.1 %.

Claim 36 (Currently Amended): Olanzapine prepared according to the processes disclosed in claim 1 that contains ~~a detectable amount, if any,~~ of less than 0.05 % of piperazine 1,4-bis-4-yl-(2-methyl)-10H-thieno-[2,3-b][1,5]benzodiazepine.

Claims 37-43 (Cancelled)